

### **AMENDMENTS TO THE CLAIMS**

Please amend claims 53-55, 61-66, and 70, and cancel claims 68 and 69 without prejudice. The following list of claims replaces all prior versions and lists of claims in the application.

1. (Withdrawn) A pharmaceutical composition for intranasal administration to a mammal comprising: an effective amount of an opioid, a liquid nasal carrier for the opioid; and one or more sweeteners, flavoring agents, or taste masking agents or combinations thereof, wherein the composition is preservative free and has a pH of about 3 to about 6.
2. (Withdrawn) A pharmaceutical composition according to claim 1, wherein the opioid is morphine, apomorphine, hydromorphone, oxymorphone, dihydromorphine, levorphanol, levallorphan, levophenacymorphan, norlevorphanol, nalorphine, nalbuphine, buprenorphine, butorphanol, naloxone, naltrexone, nalmexone, oxilorphan, cyclorphan, ketobemidone, fentanyl, sufentanil, alfentanil, or combinations thereof.
3. (Withdrawn) The pharmaceutical composition of claim 2, wherein the opioid is hydromorphone or a pharmaceutically acceptable salt thereof.
4. (Withdrawn) The pharmaceutical composition of claim 2, wherein the opioid is butorphanol or a pharmaceutically acceptable salt thereof.
5. - 6. (Cancelled)
7. (Withdrawn) The pharmaceutical composition of claim 1, wherein the composition contains a buffering agent.
8. (Withdrawn) A pharmaceutical composition according to claim 1, wherein the composition is a sterile solution or suspension.
9. (Cancelled)
10. (Withdrawn) A pharmaceutical composition according to claim 1, wherein the composition has a pH of about 5.0.

11. (Withdrawn) A method for providing analgesia to a subject in need thereof, the method comprising intranasally administering to the subject, using an intranasal unit-dose delivery device, a pharmaceutical composition comprising: an effective amount of butorphanol or a pharmaceutically acceptable salt thereof, and a liquid nasal carrier, wherein upon intranasal administration of the composition to a subject in an amount containing about 1.4 mg of butorphanol moiety, the subject exhibits a  $C_{\max}$  butorphanol plasma concentration of at least about 4000 pg/ml.
12. (Withdrawn) The method of claim 11, wherein the liquid nasal carrier comprises anhydrous citric acid, purified water and the composition has a pH of about 3 to about 6.
13. (Withdrawn) The method of claim 12, wherein the composition is a sterile solution or suspension.
14. - 15. (Cancelled)
16. (Withdrawn) The method of claim 12, wherein the composition has a pH of about 5.0.
17. (Withdrawn) An intranasally deliverable pharmaceutical composition comprising: an effective amount of hydromorphone or a pharmaceutically acceptable salt thereof and a liquid nasal carrier having the essential absence of a preservative, wherein upon intranasal administration of the composition to a subject in an amount containing about 1.8 mg of hydromorphone moiety, the subject exhibits a  $C_{\max}$  hydromorphone plasma concentration of at least about 4000 pg/ml.
18. (Withdrawn) An intranasally deliverable pharmaceutical composition comprising an effective amount of hydromorphone or a pharmaceutically acceptable salt thereof, and a preservative-free liquid nasal carrier comprising sodium chloride, citric acid, and water.
19. (Withdrawn) The pharmaceutical composition of claim 18, wherein the composition is a sterile solution or suspension.
20. (Withdrawn) The pharmaceutical composition of claim 18, wherein the composition has a pH of about 3 to about 6.
21. - 45. (Cancelled)

46. (Withdrawn) The pharmaceutical composition of claim 18, wherein the liquid nasal carrier comprises a buffering agent.
47. (Withdrawn) The pharmaceutical composition of claim 18, wherein the buffering agent is selected from sodium citrate, sodium acetate, sodium phosphate and mixtures thereof.
48. (Withdrawn) The pharmaceutical composition of claim 47, wherein the composition has a pH of about 3 to about 6.
49. (Withdrawn) The method of claim 11, wherein upon intranasal administration of the composition from a unit dose delivery device to a subject in an amount of the composition containing about 1.4 mg of butorphanol moiety, the subject exhibits a  $C_{\max}$  butorphanol plasma concentration of at least about 5000 pg/ml.
50. (Withdrawn) The method of claim 11, wherein upon intranasal administration of the composition from a unit dose delivery device to a subject in an amount of the composition containing about 1.4 mg of butorphanol moiety, the subject exhibits a  $T_{\max}$  butorphanol plasma concentration of about 0.083 to about 0.333 hours.
51. (Withdrawn) The method of claim 11, wherein upon intranasal administration of the composition from a unit dose delivery device to a subject in an amount of the composition containing about 1.4 mg of butorphanol moiety, the subject exhibits an AUC(0-t) butorphanol plasma concentration of about 5351 to about 17722 pg\*hr/ml.
52. (Withdrawn) The method of claim 11, wherein upon intranasal administration of the composition from a unit dose delivery device to a subject in an amount of the composition containing about 1.4 mg of butorphanol moiety, the subject exhibits:
- a  $C_{\max}$  butorphanol plasma concentration of at least about 4000 pg/ml; a  $T_{\max}$  butorphanol plasma concentration of about 0.083 to about 0.333 hours; and an AUC(0-t) butorphanol plasma concentration of about 5351 to about 17722 pg\*hr/ml.
53. (Currently Amended) An intranasal unit-dose delivery device comprising one or more sealed vessels containing a sterilized, preservative-free pharmaceutical composition, said composition comprising an effective amount of an opioid and a liquid nasal carrier, wherein upon positioning the device [[1]] 5 cm away from a laser beam detection pathway, actuating the

device to produce a spray plume perpendicular to said pathway, and detecting droplet size distribution of the spray plume with said laser beam detection pathway, the spray plume has a ~~maximum droplet size of about 2.2 to about 2.4  $\mu\text{m}$~~  Dv10 of from about 14.3  $\mu\text{m}$  to about 17.1  $\mu\text{m}$  and a Dv50 of from about 31.0  $\mu\text{m}$  to about 35.3  $\mu\text{m}$ .

54. (Currently Amended) The intranasal unit-dose delivery device of claim ~~53~~ 71 wherein the butorphanol tartrate is present in a total amount about 0.1 mg to about 10 mg.

55. (Currently Amended) The intranasal unit-dose delivery device of claim ~~54~~ 53 wherein the composition comprises a buffering agent.

56. (Previously presented) The intranasal unit-dose delivery device of claim 55 wherein the buffering agent is a salt of citrate, acetate or phosphate or combination thereof.

57. (Previously presented) The intranasal unit-dose delivery device of claim 56 wherein the buffering agent is present in the composition in a total amount of about 0.01% to about 3%, by weight.

58. (Previously presented) The intranasal unit-dose delivery device of claim 53 wherein the liquid nasal carrier comprises an aqueous diluent.

59. (Previously presented) The intranasal unit-dose delivery device of claim 58 wherein the aqueous diluent is selected from the group consisting of saline, water, dextrose or combinations thereof.

60. (Previously presented) The intranasal unit-dose delivery device of claim 59 wherein the composition further comprises a sweetening agent.

61. (Currently Amended) The intranasal unit-dose delivery device of claim 60 wherein the sweetening agent is selected from the group consisting of acacia syrup, anethole, anise oil, aromatic elixir, benzaldehyde, benzaldehyde elixir, caraway, caraway oil, cardamom oil, cardamom seed, cardamom spirit, cardamom tincture, cherry juice, cherry syrup, cinnamon, cinnamon oil, cinnamon water, citric acid, citric acid syrup, clove oil, cocoa, cocoa syrup, coriander oil, dextrose, eriodictyon, eriodictyon fluid\_extract, eriodictyon syrup, aromatic[[,]] ethylacetate, ethyl vanillin, fennel oil, ginger, ginger fluid\_extract, ginger oleoresin, dextrose, glucose, sugar, maltodextrin, glycerin, glycyrrhiza, glycyrrhiza elixir, glycyrrhiza extract,

glycyrrhiza extract pure, glycyrrhiza fluid\_extract, glycyrrhiza syrup, honey, iso-alcoholic elixir, lavender oil, lemon oil, lemon tincture, mannitol, methyl salicylate, nutmeg oil, orange bitter [[,]] elixir, orange bitter [[,]] oil, orange flower oil, orange flower water, orange oil, orange peel [[,]] bitter, orange peel sweet [[,]] tincture, orange spirit [[,]] compound, orange syrup, peppermint, peppermint oil, peppermint spirit, peppermint water, phenylethyl alcohol, raspberry juice, raspberry syrup, rosemary oil, rose oil, rose water, stronger, saccharin, saccharin calcium, saccharin sodium, sarsaparilla syrup, sarsaparilla compound, sorbitol solution, spearmint, spearmint oil, sucrose, sucralose, syrup, thyme oil, tolu balsam, tolu balsam syrup, vanilla, vanilla tincture, vanillin, wild cherry syrup, or combinations thereof.

62. (Currently Amended) The intranasal unit-dose delivery device of claim 53 wherein upon positioning the device 1 cm away from an impaction plate, actuating the device to produce a spray plume onto said impaction plate, and measuring minimum diameter of the spray pattern, the spray pattern has a minimum diameter of from about 2.0 cm to about 2.2 cm.

63. (Currently Amended) The intranasal unit-dose delivery device of claim 53 wherein upon positioning the device 1 cm away from a detection laser beam, actuating the device to produce a spray plume perpendicular to said laser beam, and detecting droplet size distribution of the spray plume, the spray plume has a Dv10 of from about 13.7 µm to about 19.8 µm.

64. (Currently Amended) The intranasal unit-dose delivery device of claim 53 wherein upon positioning the device 1 cm away from a detection laser beam, actuating the device to produce a spray plume perpendicular to said laser beam, and detecting droplet size distribution of the spray plume, the spray plume has a Dv50 of from about ~~20.31~~ 35.7 µm to about 55.67 µm.

65. (Currently Amended) The intranasal unit-dose delivery device of claim 53 wherein upon positioning the device 1 cm away from a detection laser beam detection, actuating the device to produce a spray plume perpendicular to said laser beam, and detecting droplet size distribution of the spray plume, the spray plume has a span as defined by Dv90-Dv10/Dv50 of about 1.55 to about 1.91.

66. (Currently Amended) The intranasal unit-dose delivery device of claim 53 wherein upon positioning the device 5 cm away from an impaction plate, actuating the device to produce a

spray pattern onto said impaction plate, and measuring maximum diameter of the spray pattern, the spray pattern has a maximum diameter of from about 7.0 cm to about 8.4 cm.

67. (Previously presented) The intranasal unit-dose delivery device of claim 53 wherein upon positioning the device 5 cm away from an impaction plate, actuating the device to produce a spray pattern onto said impaction plate, and measuring maximum diameter of the spray pattern, the spray pattern has a minimum droplet size of from about 5.8 µm to about 8.0 µm.

68. - 69. (Cancelled).

70. (Currently Amended) The intranasal unit-dose delivery device of claim 53 wherein upon positioning the device 5 cm away from a detection laser beam, actuating the device to produce a spray plume perpendicular to said laser beam, and detecting droplet size distribution of the spray plume, the spray plume has a span as defined by Dv90-Dv10/Dv50 of about 1.5 to about 1.9.

71. (Previously presented) The delivery device of claim 53 wherein the opioid is butorphanol tartrate.

72. (Previously presented) The delivery device of claim 71 wherein nasal carrier is citrate buffered water, and the composition contains sucrose.